# Selective Activation of Small Motor Axons by Quasitrapezoidal Current Pulses

Zi-Ping Fang and J. Thomas Mortimer

*Abstract*—**We have found a method to activate electrically smaller nerve fibers without activating larger fibers in the same nerve trunk. The method takes advantage of the fact that action potentials are blocked with less membrane hyperpolarization in larger fibers than in smaller fibers. In our nerve stimulation system, quasitrapezoidal-shaped current pulses were delivered through a tripolar cuff electrode to effect differential block by membrane hyperpolarization. The quasitrapezoidal-shaped pulses with a square leading edge, a 350 μs plateau, and an exponential trailing phase ensured the block of propagating action potentials and prevented the occurrence of anodal break excitation. The tripolar cuff electrode design restricted current flow inside the cuff and thus eliminated the undesired nerve stimulation due to a "virtual cathode." Experiments were performed on 13 cats. The cuff electrode was placed on the medial gastrocnemius nerve. Both compound and single fiber action potentials were recorded from *L7* ventral root filaments. The results demonstrated that larger alpha motor axons could be blocked at lower current levels than smaller alpha motor axons, and that all alpha fibers could be blocked at lower current levels than gamma fibers. A statistical analysis indicated that the blocking threshold was correlated with the axonal conduction velocity or fiber diameter. This method could be used in physiological experiments and neural prostheses to achieve a small-to-large recruitment order in motor or sensory systems.**

## INTRODUCTION

In neuroprosthesis design and neurophysiology research, it is often desirable to be able to activate selectively a certain population of nerve fibers in a nerve trunk without concomitant excitation of the others. Since larger nerve fibers have lower excitation threshold to extracellular stimulus [14], the challenge is to activate smaller fibers without the involvement of the larger ones.

Since 1979, we have published on work concerning the generation of unidirectionally propagated action potentials for implementing collision block in peripheral nerves [13], [16]-[20]. Several asymmetric cuff electrode designs and quasitrapezoidal current pulses were studied for effectively blocking the action potential at one end of the cuff by transient hyperpolarization of the nerve membrane. While the objective of these studies was to achieve a complete blockage of action potential propagation in one direction, we have found that this technique can be utilized to obtain differential neural block and thus effect selective activation of small nerve fibers as well.

In this paper we present a description of the new stimulation method for selective activation of small nerve fibers. A model analysis is presented to predict the behavior of the differential block with membrane hyperpolarization. Results from animal experiments verify the proposed technique. Preliminary accounts of these results have been presented elsewhere [4].

## METHODS

### Electrode Design

A tripolar spiral cuff electrode was fabricated and employed in animal experiments. The general properties of the spiral cuff electrode have been reported [12]. Therefore, only the specific configuration of the electrode used in this work is to be described here. As shown in Fig. 1, the spiral silicone rubber cuff had an inner diameter of 1.5 mm and was placed onto a nerve trunk of about 1.0 mm diameter. The spiral cuff was self-curling and had one and one half to two wraps to prevent current leakage while still being easy to install. The stimulating surfaces were three platinum rings with an exposed width of about 0.5 mm. The interpolar distance was 8 mm on both sides, resulting in a total cuff length of about 20 mm. The center ring acted as a cathode to excite the nerves by membrane depolarization. The two outer rings were connected together and served as anodes to block the nerves by membrane hyperpolarization. This symmetrical tripolar design restricted the stimulus current to the inside of the cuff and consequently prevented the undesired nerve excitation that might be elicited by a "virtual cathode" [16], [19].

### Stimulus Waveform

The stimuli employed in this work for effecting differential neural block were quasitrapezoidal-shaped current pulses [18]. These current pulses consisted of a square leading edge and a plateau phase of approximately 350 μs followed by an exponential trailing phase with a fall time (90–10%) of approximately 600 μs, as shown in Fig. 1. The relatively wide pulse width ensured that the membrane would be hyperpolarized until the depolarizing current from the neighboring nodes subsided. The exponential decay was necessary to prevent excitation due to the "anodal break" phenomenon. The specific shape and duration of the current pulse were selected to minimize the total charge injection to the system [16], [19].

## MODEL PREDICTION

### The Model

A model analysis was performed to predict the differential blocking effect of the proposed technique. The electrical field of the cuff electrode, the nerve model of a myelinated axon, and the interaction between the two were examined.

The electrical field profile of a cuff electrode had been studied by Altman and Plonsey [3]. Through model analysis, they found

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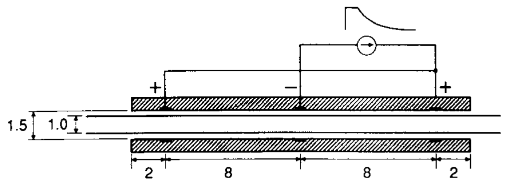
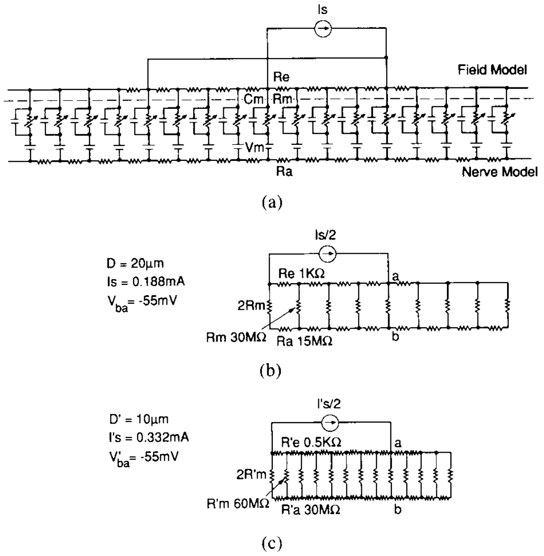


Fig. 1. Electrode configuration and stimulus waveform. In the transverse cross-section of the cuff electrode, the hatched parts represent the silicone rubber sheath and the dark parts represent the platinum rings. The center conducting ring was used as the cathode and the other two were used as anodes. Dimensions are in millimeters. The stimuli were quasitrapezoidal-shaped current-regulated pulses with a square leading edge, a plateau pulse width of approximately 350 $\mu$s and an exponential trailing phase with a fall time (90–10%) of approximately 600 $\mu$s.

that the ring electrode in a cuff could be approximated as a disk electrode to simplify the problem without introducing significant error. The field model in the present work was based on this approximation. As shown in Fig. 2(a), the extracellular potential was simply determined by the product of the extracellular resistance and the current flowing inside the cuff. The extracellular resistance depended on the cuff and axon diameter, the resistivity of the fluid in the medium, and the axial length. For a 1.5 mm cuff inner diameter, a 1.0 mm nerve trunk diameter, and a 50 Ω-cm resistivity of the saline bath, the axial extracellular resistance was about 500 Ω/mm, or 4 kΩ between the anode and the cathode with an interpolar distance of 8 mm. The current flowing through the extracellular space was half of the current provided by the stimulator and no current would flow outside the cuff because of the symmetrical tripolar cuff configuation.

The nerve model shown in Fig. 2(a) is a standard cable model of myelinated axon [11]. While it has been widely used to study excitation phenomena, this dynamic model is difficult to solve due to the nonlinear membrane impedance [11]. In some cases, a simpler model was used to analyze the effect of certain stimuli [1]. In this steady-state model, the membrane resistance was fixed at a constant value, the membrane capacitance was eliminated, and an "excitation threshold" of 15 mV membrane depolarization was used. A comparison of threshold calculated from a steady-state and a dynamic model of a myelinated nerve fiber has been published [15]. It was concluded that these models compared favorably for stimulus pulse durations of 100 $\mu$s or longer.

Since the main purpose of the present work was to analyze the action potential block by membrane hyperpolarization with wide pulses (pulse width > 350 $\mu$s), the above steady-state model was considered to be adequate. The cable model of Fig. 2(a) was thus simplified to the form of Fig. 2(b). First, the time and voltge dependent membrane impedance was replaced by a constant resistance because of the use of wide pulses. This simplification could also be justified because simulation results from a model using the Frankenhaeuser–Huxley nonlinear equations indicated that the membrane resistance was constant during hyperpolarization [3]. Second, the batteries of the resting potential were removed because only the deviation from the resting potential should be taken into account. Third, the model was reduced to half of the complete form because of the system symmetry; note that the current injection was halved and that the membrane resistance of the center node was doubled so that the voltage drop across each resistance element in the "half model" would be equivalent to those in the "complete model".



(a)

(b)

(c)

Fig. 2. Models representing the cuff electrode-nerve fiber system. (a) A complete model showing a 20 $\mu$m myelinated axon coupled with the electrical field of a cuff electrode. $R_e$ is the extracellular resistance between two neighboring nodes that are enclosed in the cuff sheath. Other circuit elements are the same as in reference [11]. (b) A simplified model for calculating the blocking threshold of a 20 $\mu$m fiber. (c) A simplified model for calculating the blocking threshold of a 10 $\mu$m fiber.

When the field model was coupled to the nerve model, it was obvious that the node beneath the center cathode should be depolarized the most, and the nodes beneath the two anodes should be hyperpolarized the most by the injected current. Similar to the membrane excitation threshold of 15 mV depolarization [1], there should be a "membrane blocking threshold," i.e., once the membrane hyperpolarization exceeded this value, the action potential conduction would fail. In experimental results documented by van den Honert [17] where membrane potential was recorded from a single node of Ranvier using the potentiometric technique, it was shown that as the membrane of a node was hyperpolarized to about 60 mV lower than the resting potential, an invading action potential failed to excite the node. Similarly, in simulation results reported by Altman and Plonsey [3], where membrane behavior was simulated by the Frankenhauser–Huxley equations, it was presented that when the transmembrane potential at a node was shifted to about 50 mV lower than the resting potential, excitation initiated at neighboring nodes failed to propagate through the node. Based on these experimental and simulation data, a membrane blocking threshold of −55 mV was adopted in the present study. This criterion would be used in the following calculation to estimate the "system blocking threshold," which was defined as the pulse current strength just strong enough to effect a conduction block for a nerve group of certain fiber diameter.

### *Effect of Fiber Diameter*

The model constructed in the previous section was utilized to estimate the current strength for blocking the nerve fibers of different diameters. The parameters of the model were those that had been widely used in the literature [11]. The internodal length was chosen as 100 times the fiber diameter [10], resulting in an internodal length of 2 mm for a 20 $\mu$m diameter fiber

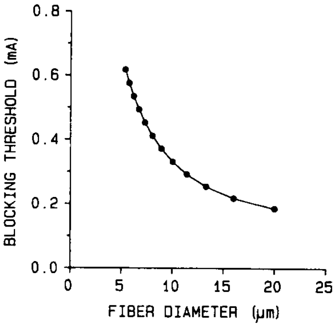


Fig. 3. Blocking threshold as a function of fiber diameter predicted by the model analysis. It was predicted that the larger fibers would be blocked at lower current strength by membrane hyperpolarization.

[Fig. 2(b)], and an internodal length of 1 mm for a 10 $\mu$m fiber [Fig. 2(c)]; and there were four and eight internodes between each pair of conducting rings, respectively. The pulse current strength that would hyperpolarize the membrane to 55 mV lower than the resting potential were calculated to obtain the "system blocking threshold" or "blocking threshold." The numerical computation was performed on an IBM AT computer for many network configurations. The computation results for the fibers of 5–20 $\mu$m diameter are summarized in Fig. 3. The results obtained using this model predict that larger fibers have a lower blocking threshold than do smaller fibers. This is because the internodal voltage required to effect block is almost the same for all the fibers so the more nodes there are between the anode and cathode the higher the required interpolar voltage or injecting current to effect block.

## EXPERIMENTAL PROCEDURE

### *Animal Preparation*

Acute experiments were performed on thirteen adult cats weighing 2.4–4.0 kg. The animals were anesthetized with IM ketamine hydrochloride (30 mg/kg), then maintained on IV sodium pentobarbital (10 mg increments as needed). All animals were intubated and IM atropine sulfate (0.044 mg/kg) was administered to reduce salivation.

The experimental setup is illustrated in Fig. 4. The tibia was immobilized in a stereotaxic frame by clamps at both ends of the bone. The sciatic nerve was exposed in the popliteal fossa, and the branch innervating the medial gastrocnemius was surgically isolated for a length of about 4 cm to install the cuff electrode. The nerve and muscle were bathed in lactated Ringer's solution. The temperature of the bath was maintained by radiant heat at 37°C. After laminectomy, the ipsilateral *L*7 ventral root was separated and placed onto a pair of hook electrodes to record both compound and single fiber action potentials. For recording single fiber action potentials, fine filaments containing one to several active alpha and/or gamma fibers were divided from the ventral root under a surgical microscope using watch-makers forceps.

### *Stimulation and Recording*

The quasitrapezoidal-shaped, current-regulated pulses for effecting differential block were generated by a battery-powered stimulator. The stimulator could also generate narrow rectangular current pulses to stimulate nerve fibers in a conventional way. The width of the rectangular stimulus was set at 10 $\mu$s to obtain better amplitude threshold separation between larger and smaller fibers [8]. A pair of silver-silver chloride hooks with an interpolar distance of 5 mm was used to record both compound and single fiber action potentials. The recording electrodes were connected to a digital storage oscilloscope through a battery-powered preamplifier.

During compound or single fiber action potential recordings, the quasitrapezoidal and the narrow rectangular pulses were applied alternatively and with varying amplitude. The blocking threshold and activation threshold were recorded for each fiber or fiber group. The axonal conduction velocity was calculated from the conduction delay between a 10 $\mu$s rectangular stimulus and the front edge of an action potential in all tests.

## RESULTS

### *Compound Action Potential Recordings*

Compound action potentials were recorded from *L*7 ventral root in eight animals. In Fig. 5 is shown a typical recording from one of the animals tested. The left column shows the recruitment process with narrow rectangular stimuli. As the stimulis amplitude increased, the fast alpha volley, then the slow alpha volley, and finally the gamma volley appeared in sequence. The results confirm what has been previously reported, namely the large fibers are excited at lower stimulus current and one can not selectively activate small fibers by using the conventional stimulation scheme.

In the right column of Fig. 5 is shown the differential blocking process when the quasitrapezoidal pulses were applied. All nerve fibers were excited when the pulse amplitude exceeded the activation threshold of about 0.1 mA for the pulse width used. As the pulse magnitude was raised higher than the blocking threshold of about 1.0 mA, the amplitude of the mass alpha volley gradually decreased and the latency gradually increased. At an even higher pulse magnitude, 3.7 mA in this case, the alpha volley was completely suppressed, sparing only gamma fiber activities. All the recordings in the eight animals studied exhibited the same trend, i.e., the fast components were blocked before the slow ones in the alpha group, and the alpha volley was blocked without affecting most of the gamma volley. However, the current amplitude to effect the differential block varied considerably between different preparations. As an example, the current amplitude at which the alpha volley was completely suppressed ranged from 1.0 to 3.8 mA, with an average of 2.5 mA, in the eight preparations tested. This was probably caused by the difference in the tightness of the cuff and the influence of the connective tissue between the cuff and the fibers. The implication of these results on the chronic application of the technique is that the blocking threshold current may change during the initial stage of an implantation when connective tissue grows between the electrode conductors and the nerve fibers, similar to what happens for excitation threshold in conventional stimulation schemes.

### *Single Fiber Action Potential Recordings*

To further investigate the order of differential blocking, action potentials were recorded from the ventral root filaments containing only two alpha fibers or one alpha and one gamma fiber that could be activated. In Fig. 6 is shown a typical recording from a pair of alpha fibers. Using a low amplitude 10 $\mu$s rectangular pulse, only the fast fiber was excited. At a higher

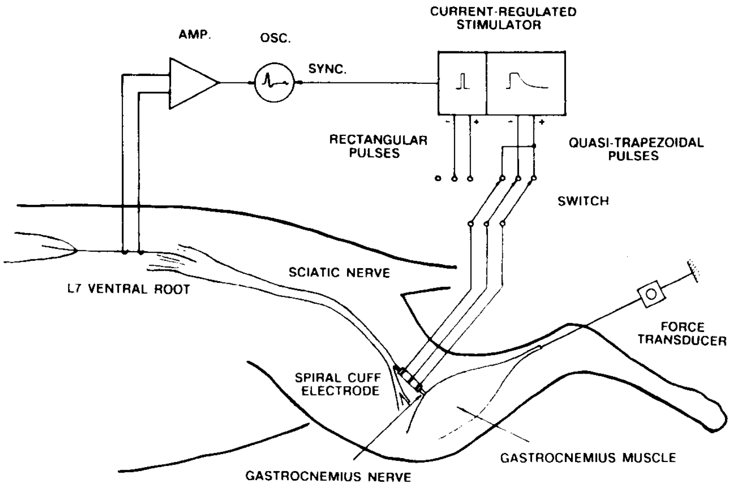


Fig. 4. Experimental setup. The sciatic nerve was exposed in the popliteal fossa. A tripolar spiral cuff electrode was installed on the medial gastrocnemius nerve branch. A current-regulated stimulator that generates both wide quasitrapezoidal and narrow rectangular pulses was connected to the cuff electrode through a selection switch. The $L7$ ventral root was exposed by laminectomy. A pair of hook electrode was employed to record compound and single fiber action potentials. The signal was amplified by an battery-powered preamplifier and displayed on a digital oscilloscope.

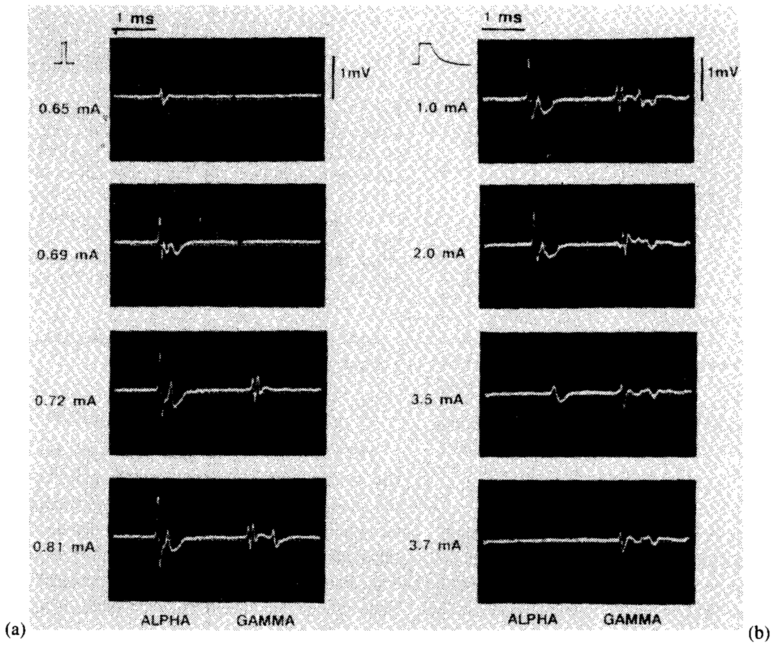


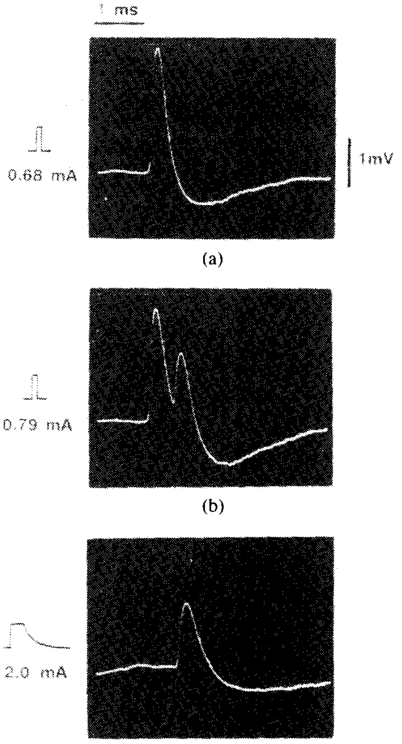
Fig. 5. Compound action potential recordings from $L7$ ventral root. (a) Recruitment process with 10 $\mu$s rectangular stimuli. As the stimulus amplitude increased, the faster alpha volley, the slower alpha volley, and finally the gamma volley appeared in sequence. (b) Differential blocking process with 350 $\mu$s quasitrapezoidal pulses. As the stimulus amplitude increased, the amplitude of the mass alpha volley gradually decreased and the latency increased, implying a large-to-small blocking order. The onset time for the stimulus is coincident with the beginning of each trace.

stimulus level, the slow fiber was activated and both fibers were firing. When the 350 $\mu$s quasitrapezoidal pulse with an appropriate amplitude was applied, the first spike could be suppressed, while sparing the second spike. This result demonstrated the feasibility of selective activation of small alpha fibers with the proposed method. In Fig. 7 is shown a typical recording from a nerve filament with an alpha fiber and a gamma fiber. Here the alpha fiber was activated at a lower stimulus strength and also blocked at a lower current level than was the gamma fiber. This result indicated that gamma fibers could be selectively activated at appropriate pulse amplitudes.

All observations obtained from single action potential recordings are listed in Table I. It can be seen that in 45 pairs of fast-slow alpha fibers tested, the faster fibers were blocked at lower blocking current level in 42 pairs. This ratio is significantly different from random distribution ($P < 0.001$). In the 27 pairs of alpha and gamma fibers tested, selective activation of the gamma fibers was demonstrated in 22 pairs. This ratio is also significantly different from random distribution.($P < 0.001$).

### *Relationship between Blocking Threshold and Conduction Velocity*

In an attempt to describe quantitatively the relationship between blocking threshold and axonal conduction velocity, re-



(a)

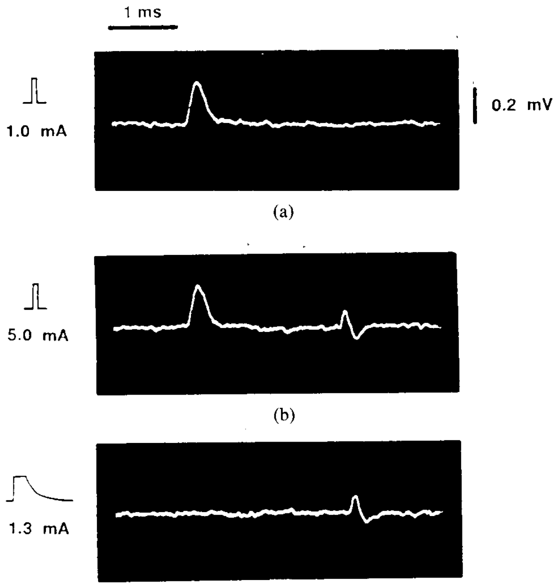
(b)

(c)

Fig. 6. Single fiber action potentials recorded from a fine filament containing two active alpha fibers (conduction velocities of 109 and 80 m/s). (a) The faster fiber had an activation threshold of 0.58 mA with the 10 μs rectangular stimulus. (b) The slower fiber had an activation threshold of 0.77 mA. With a 0.79 mA, 10 μs stimulus, both fibers were activated. (c) When the 350 μs quasitrapezoidal pulse was applied, the faster and slower fiber had a blocking threshold of 1.9 and 2.1 mA, respectively. With a 2.0 mA pulse, the faster fiber was blocked, while the slower one fired. The onset time for the stimulus is coincident with the beginning of each trace.

cordings were made from 16 single alpha axons and seven single gamma axons in a single animal under exactly the same conditions. Data from the alpha group are plotted in Fig. 8(a). As can be seen from the plot, the larger axons were blocked at lower current level. The straight line shown in the figure is the least-mean square fitting line. The slope of the line is $-0.010 \pm 0.002$ (mean ± S.E. of the mean). This slope is significantly different from zero ($P < 0.001$). The linear correlation coefficient between the blocking threshold and the conduction velocity is $-0.75$, and it is significantly different from zero ($P < 0.001$). The Kendall rank-order correlation coefficient for the same set of data is $-0.56$, which is also statistically significant ($P < 0.001$). The correlation between the activation threshold and the axon conduction velocity is also shown in Fig. 8(b) for the purpose of comparison.

In Fig. 9(a) data from alpha and gamma fibers are presented together. The linear correlation between the blocking threshold and the conduction velocity was high ($r = -0.84$) for the whole data pool, but not within the gamma group. However, it is worth noting that when the current amplitude was raised to a level to block all the alpha fibers, none of the gamma fibers were affected. In other words, it is possible to activate selectively the gamma population with this stimulation scheme. The comparison of activation threshold for the two groups of fibers is also shown in Fig. 9(b).



(a)

(b)

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Fig. 7. Single fiber action potentials recorded from a fiber filament containing one active alpha fiber (120 m/s) and one gamma fiber (40 m/s). (a) The alpha fiber had an activation threshold of 0.3 mA with the 10 μs rectangular stimulus. (b) The gamma fiber had an activation threshold of 1.5 mA. With a 5 mA, 10 μs stimulus, both fibers were activated. (c) When the 350 μs quasitrapezoidal pulse was applied, the alpha and gamma fiber had a blocking threshold of 1.0 and 1.6 mA, respectively. With a 1.3 mA pulse, the alpha fiber was blocked, while the gamma fiber fired. The onset time for the stimulus is coincident with the beginning of each trace.

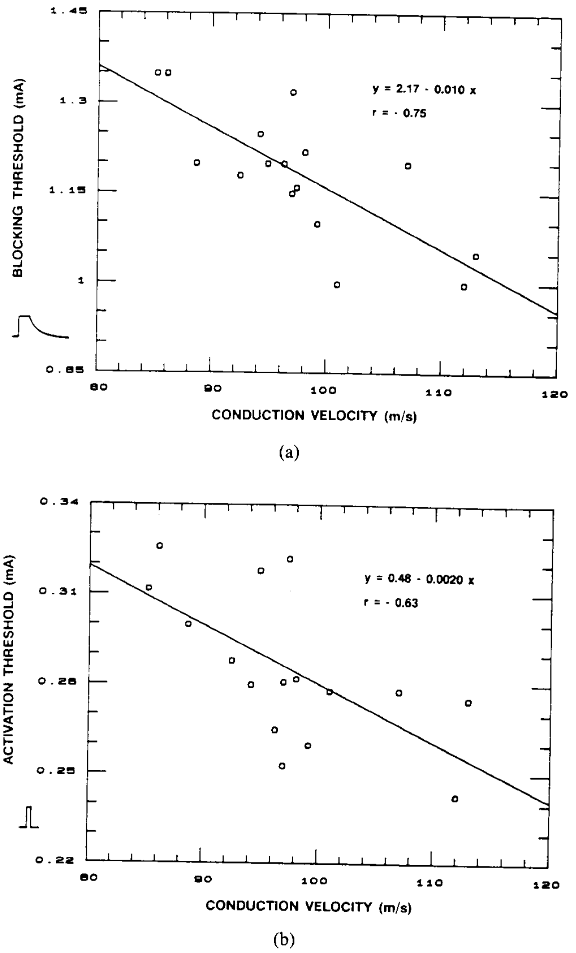
## DISCUSSION

The central problem in this work was to investigate whether the technique developed previously for the generation of unidirectionally propagated action potentials could be used for selective activation of small nerve fibers. The experimental results showed that in most cases smaller alpha fibers could be activated without activation of larger alpha fibers, and gamma fibers could be selectively excited without discharge of alpha fibers. However, the selectivity of the system was not perfect and there were some exceptions. The variation could be induced by the uneven field of the cuff electrode; the different locations of the nodes relative to the electrode; the variabilities of internodal length as a function of axon diameter or conduction velocity, etc. In their experiments on the "size principle" of motor unit recruitment under physiological activation, Henneman et al. found that there were some exceptions, or "reversed recruitment" [9]. For the 165 pairs of motoneurons tested in their study, the recruitment order of small-to-large alpha fiber was observed in 142 pairs. Therefore, for functional application, the peripheral stimulation scheme presented here will do no worse in size order recruitment than the central nervous system does.

The present results are similar to what was reported by Fukushima *et al.* [7]. In their experiments with the motor system, dc polarizing current was applied between stimulation and recording sites to effect differential block. Eighteen out of the 26 *L7* ventral root filaments showed consecutive blocking from thicker to thinner fibers with increase of polarizing current. The

TABLE I
SUMMARY OF SINGLE FIBER RECORDING RESULTS. DATA COLLECTED FROM SEVEN ANIMALS. AMONG THEM, RECORDINGS FOR ALPHA–GAMMA PAIRS WERE ONLY PERFORMED IN FOUR ANIMALS

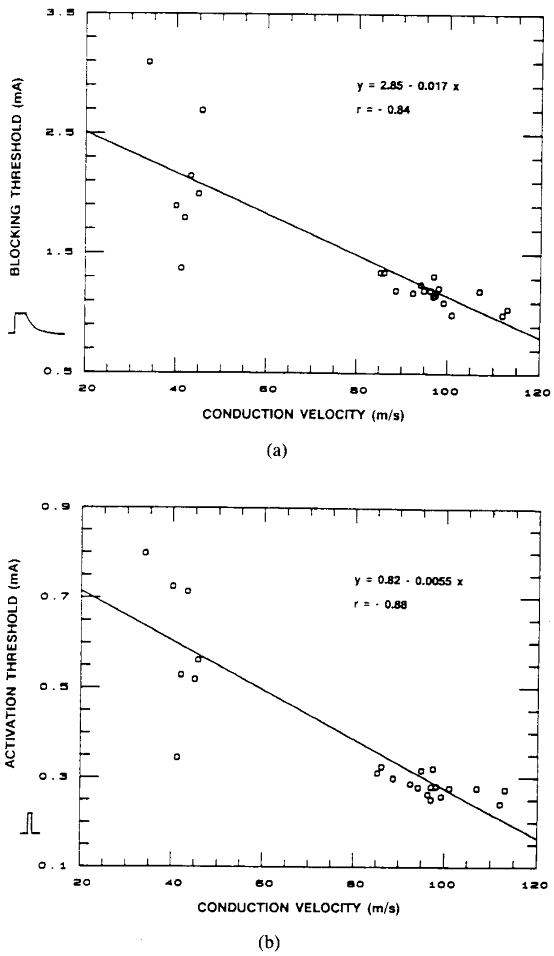
| | Number of Fiber Pairs | | | | | |
|---|---|---|---|---|---|---|
| | Fast-Slow Alpha Pair | | | Alpha-Gamma Pair | | |
| Experiment | Fast Blocked Before Slow | Slow Blocked Before Fast | Total | Alpha Blocked Before Gamma | Gamma Blocked Before Alpha | Total |
| 1 | 7 | 0 | 7 | — | — | — |
| 2 | 2 | 0 | 2 | 5 | 1 | 6 |
| 3 | 6 | 0 | 6 | 11 | 0 | 11 |
| 4 | 8 | 0 | 8 | — | — | — |
| 5 | 3 | 0 | 3 | 5 | 0 | 5 |
| 6 | 7 | 1 | 8 | — | — | — |
| 7 | 9 | 2 | 11 | 1 | 4 | 5 |
| Total | 42 | 3 | 45 | 22 | 5 | 27 |



(a)

(b)

Fig. 8. Relationship between threshold and conduction velocity for sixteen alpha fibers in a nerve trunk. (a) Correlation between blocking threshold and conduction velocity. (b) Correlation between activation threshold and conduction velocity.



(a)

(b)

Fig. 9. Comparisons of threshold distribution for sixteen alpha fibers and seven gamma fibers in a nerve trunk. (a) Comparison of blocking threshold for the two groups of fibers. Note all gamma fibers had higher blocking threshold than those of alpha fibers. (b) Comparison of activation threshold for the two groups of fibers. Also all gamma fibers had higher activation threshold than those of alpha fibers.

disadvantage of dc block is that the current has to be applied gradually to prevent neural firing prior to block, and direct current would cause serious neural tissue damage if it was applied for any reasonable period of time. Acconero *et al.* achieved differential block in sensory nerve fibers by employing triangularly shaped pulses [2]. Although the triangular pulses are easier to generate, they may not be as efficient as the quasitrapezoidal pulses in maintaining the membrane hyperpolarization until the depolarizing current from the neighboring area subsides. The duration of their pulses is one order of magnitude longer than that of ours. Large charge injection due to the longer pulse duration in their case is again unfavorable for chronic application. Compared to dc and triangular pulse techniques, the method examined in this work suggested a similar or better activation selectivity with the least charge delivery. These properties are crucial in chronic animal and patient usage where reliable long-term performance is demanded.

The quasitrapezoidal stimuli used in this work were monophasic current pulses. For long-term application charge-balanced biphasic current pulses should be employed to prevent the adverse effects of electrochemical reactions induced by the stimuli. While biphasic quasitrapezoidal pulses have not been used in the recruitment order tests, previous study concerning the generation of unidirectionally propagated action potentials has demonstrated that charge-balanced biphasic pulses can effect anodal block in a similar way as monophasic pulses [20]. Further work is necessary to characterize the frequency dependence of the scheme with biphasic stimuli and to optimize the parameters for charge-balanced biphasic current pulses.

The technique for selective activation of small nerve fibers should have a wide range of application in both basic research and clinical practice. We have explored the possibility of utilizing this method to achieve physiological recruitment order of small-to-large motor units in electrically activated muscles [5]. A more detailed description of this particular application is presented in a companion paper [6].

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